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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,286	02/03/2005	Christopher J. Dinsmore	21007YP	3804
210	7590	11/08/2006		
MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907			EXAMINER CHU, YONG LIANG	
			ART UNIT	PAPER NUMBER
			1626	

DATE MAILED: 11/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/523,286	Applicant(s) DINSMORE ET AL.	
	Examiner Yong Chu	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 7-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 6 is/are rejected.
- 7) ☒ Claim(s) 1-6 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>9/26/2006</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-2, 4 are amended by the Amendment filed on 26 September 2006.

Claims 1-19 are pending. Claims 7-19 remain withdrawn. Therefore, claims 1-6 will be examined on the merits.

Response to Restriction requirement

Applicant has amended the claims 1 and 2 in accordance with the restriction requirement.

Response to Amendment

The Amendments by Applicants' representative Michael E. Carmen dated on 26 September 2006 has been entered.

Response to Argument

Claim objections

The objection over claims 1 and 4 has been withdrawn after considering the changes made by Applicant in accordance with the Examiner's suggestion.

Argument over rejection of claims under 35 U.S.C. §103(a)

Applicant's arguments over rejection of claims 1-6 under 35 U.S.C. §103(a) have been considered, are found persuasive.

Applicant's argument is on the ground that the cited prior art US Patent 5,527,819 ('819) is non-analogous art, because the reference is related to inhibitors of HIV reverse transcriptase, and not reasonably pertinent to the current invention of inhibiting tyrosine kinases for cancer treatment. This argument is persuasive, and the rejection of claims 1-6 under 35 U.S.C. §103(a) has been withdrawn.

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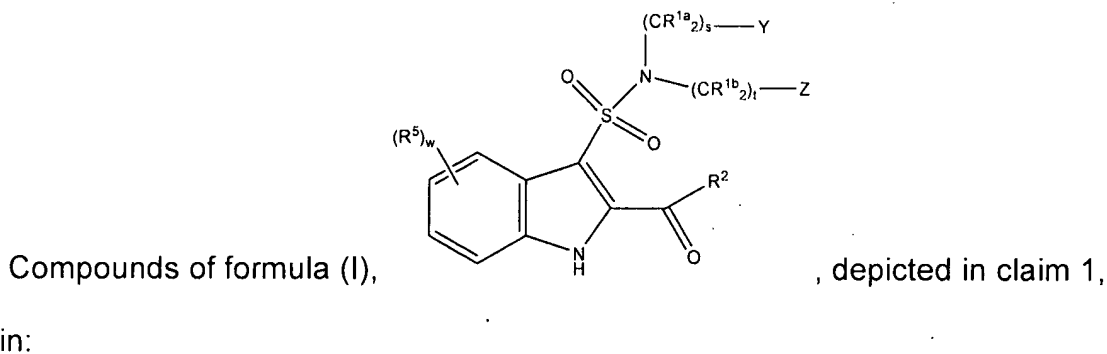
Double patenting

The rejection over claims 1-6 under double patenting over '819 patent has been withdrawn for the reason stated supra. However, upon further search and/or consideration, a new ground(s) of rejection is made in view of US Patent 3180875 ('875).

Because of the new prior art, a new restriction requirement is need to reflect the elected species and the reasonable scope of invention.

Status of the Claims

The new scope of invention searched and examined as follows:



R^{1a} and R^{1b} are independently selected from hydrogen, unsubstituted and substituted C_1 - C_{10} alkyl;

R^{1c} is independently selected from: hydrogen, C_1 - C_{10} alkyl; OR^3 , $N(R^3)_2$, and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^2 is independently selected from $N(R^3)_2$, and OR^3 ;

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R^3 is independently selected from hydrogen and C_1 - C_{10} alkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^6 is independently selected from C_1 - C_{10} alkyl and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^7 is independently selected from hydrogen, unsubstituted or substituted C_1 - C_{10} alkyl, unsubstituted or substituted C_3 - C_{10} cycloalkyl, halogen, CF_3 , CN, and NO_2 ;

Y is hydrogen;

Z is hydrogen, $S(O)_mN(R^3)_2$ or $C(O)N(R^3)_2$;

s is 0;

t is 0 to 6;

m is 2;

n is 0 to 6;

w is 0 to 4; and

R^5 is defined in claim 1.

As a result of the election and the corresponding scope of the invention identified supra, the remaining subject matters of claims 1-6 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being drawn to non-elected inventions.

The subject matter which are withdrawn from consideration as being non-elected subject differ materially in structure and composition and have been restricted properly a reference which anticipated but the elected subject matter would not even render obvious the withdrawn subject matter and the fields of search are not co-extensive.

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Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, and 6 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The substituents R^3 and R^7 are indefinite because they are defined as mutual dependent, and therefore indefinite.

Claim Rejections - 35 USC § 102(b)

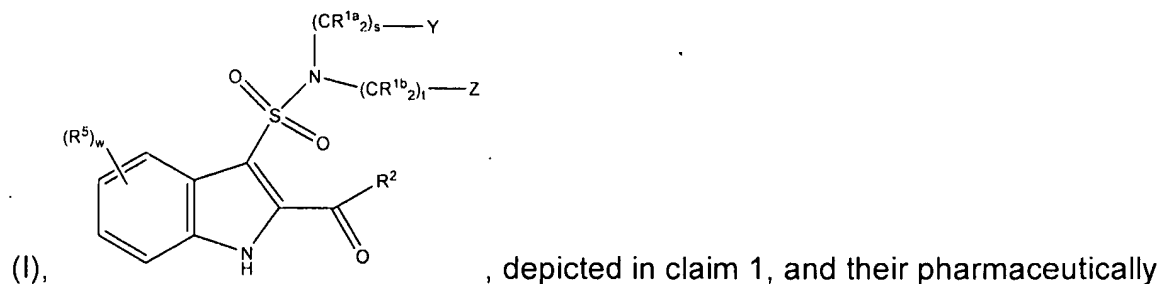
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 6 are rejected under 35 U.S.C. 102 (b) as being anticipated by Szmuszkovicz, U.S. Patent No. 3,180,875 (1965).

Applicants' instant elected invention in claims 1-3 teach compounds of formula



acceptable salts and pharmaceutical composition thereof wherein:

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R^{1a} and R^{1b} are independently selected from hydrogen, unsubstituted and substituted C_1 - C_{10} alkyl;

R^{1c} is independently selected from: hydrogen, C_1 - C_{10} alkyl; OR^3 , $N(R^3)_2$, and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^2 is independently selected from $N(R^3)_2$, and OR^3 ;

R^3 is independently selected from hydrogen and C_1 - C_{10} alkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^6 is independently selected from C_1 - C_{10} alkyl and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^7 is independently selected from hydrogen, unsubstituted or substituted C_1 - C_{10} alkyl, unsubstituted or substituted C_3 - C_{10} cycloalkyl, halogen, CF_3 , CN , and NO_2 ;

Y is hydrogen;

Z is hydrogen, $S(O)_mN(R^3)_2$ or $C(O)N(R^3)_2$;

s is 0;

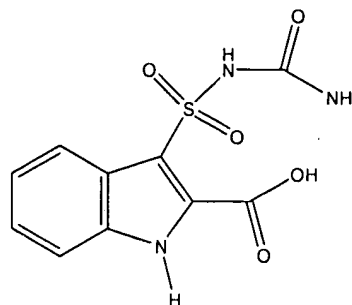
t is 0 to 6;

m is 2;

n is 0 to 6;

w is 0 to 4; and

R^5 is defined in claim 1.



Szmuszkovicz discloses a specific compound

(CAS CN

875830-38-9). This prior art compound reads on the instantly claimed genus, wherein:

R^{1a} and R^{1b} are independently selected from hydrogen, unsubstituted and substituted C_1 - C_{10} alkyl;

R^{1c} is independently selected from: hydrogen, C_1 - C_{10} alkyl; OR^3 , $N(R^3)_2$, and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^2 is OR^3 , wherein R^3 is hydrogen;

R^6 is independently selected from C_1 - C_{10} alkyl and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^7 is independently selected from hydrogen, unsubstituted or substituted C_1 - C_{10} alkyl, unsubstituted or substituted C_3 - C_{10} cycloalkyl, halogen, CF_3 , CN, and NO_2 ;

Y is hydrogen;

Z is $C(O)N(R^3)_2$, wherein R^3 is hydrogen;

s is 0;

t is 0;

m is 2;

n is 0 to 6;

w is 0; and

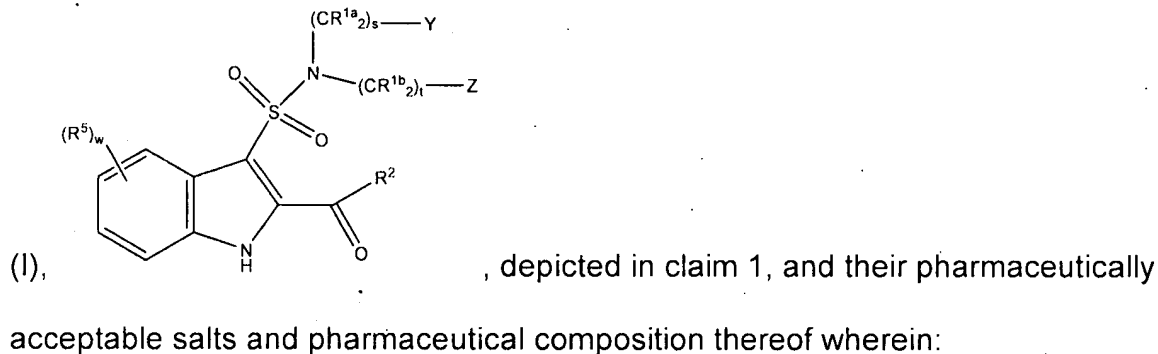
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R^5 is defined in claim 1.

Since the compounds are anticipated, the pharmaceutical composition comprising the claimed compound is also anticipated.

Claims 1-3, and 6 are rejected under 35 U.S.C. 102 (b) as being anticipated by Szmuszkovicz, *Journal of Organic Chemistry* (1964), 29(1), p178-84.

Applicants' instant elected invention in claims 1-3 teach compounds of formula



R^{1a} and R^{1b} are independently selected from hydrogen, unsubstituted and substituted C_1 - C_{10} alkyl;

R^{1c} is independently selected from: hydrogen, C_1 - C_{10} alkyl; OR^3 , $N(R^3)_2$, and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^2 is independently selected from $N(R^3)_2$, and OR^3 ;

R^3 is independently selected from hydrogen and C_1 - C_{10} alkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^6 is independently selected from C_1 - C_{10} alkyl and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

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R^7 is independently selected from hydrogen, unsubstituted or substituted C_1 - C_{10} alkyl, unsubstituted or substituted C_3 - C_{10} cycloalkyl, halogen, CF_3 , CN, and NO_2 ;

Y is hydrogen;

Z is hydrogen, $S(O)_mN(R^3)_2$ or $C(O)N(R^3)_2$;

s is 0;

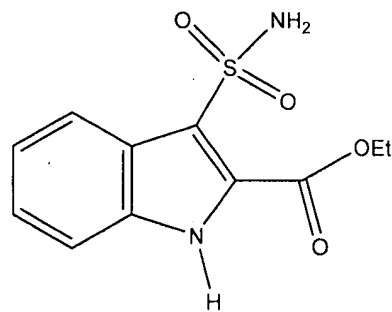
t is 0 to 6;

m is 2;

n is 0 to 6;

w is 0 to 4; and

R^5 is defined in claim 1.



(CAS

Szmuszkovicz discloses a specific compound

CN 91088-34-5). This prior art compound reads on the instantly claimed genus,

wherein:

R^{1a} and R^{1b} are independently selected from hydrogen, unsubstituted and substituted C_1 - C_{10} alkyl;

R^{1c} is independently selected from: hydrogen, C_1 - C_{10} alkyl; OR^3 , $N(R^3)_2$, and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^2 is OR^3 , wherein R^3 is ethyl group;

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R^6 is independently selected from C_1 - C_{10} alkyl and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ; R^7 is independently selected from hydrogen, unsubstituted or substituted C_1 - C_{10} alkyl, unsubstituted or substituted C_3 - C_{10} cycloalkyl, halogen, CF_3 , CN, and NO_2 ;

Y is hydrogen;

Z is hydrogen;

s is 0;

t is 0;

m is 2;

n is 0 to 6;

w is 0; and

R^5 is defined in claim 1.

Since the compounds are anticipated, the pharmaceutical composition comprising the claimed compound is also anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

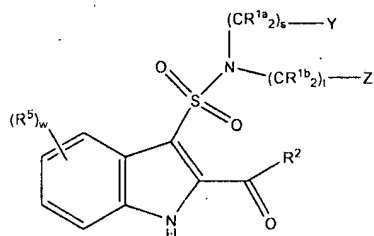
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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3 and 6 are rejected under 35 U.S.C. 103 (a) as unpatentable over Szmuszkovicz U.S. Patent 3,180,875 *in view* Szmuszkovicz, *Journal of Organic Chemistry* (1964), 29(1), p178-84.

Applicants' instant elected invention in claims 1-3 teach compounds of formula



, depicted in claim 1, and their pharmaceutically acceptable salts and pharmaceutical composition thereof wherein:

R^{1a} and R^{1b} are independently selected from hydrogen, unsubstituted and substituted C_1 - C_{10} alkyl;

R^{1c} is independently selected from: hydrogen, C_1 - C_{10} alkyl; OR^3 , $N(R^3)_2$, and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^2 is independently selected from $N(R^3)_2$, and OR^3 ;

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R^3 is independently selected from hydrogen and C_1 - C_{10} alkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^6 is independently selected from C_1 - C_{10} alkyl and C_3 - C_{10} cycloalkyl; said alkyl, cycloalkyl is optionally substituted with at least one substituent selected from R^7 ;

R^7 is independently selected from hydrogen, unsubstituted or substituted C_1 - C_{10} alkyl, unsubstituted or substituted C_3 - C_{10} cycloalkyl, halogen, CF_3 , CN, and NO_2 ;

Y is hydrogen;

Z is hydrogen, $S(O)_mN(R^3)_2$ or $C(O)N(R^3)_2$;

s is 0;

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m is 2;

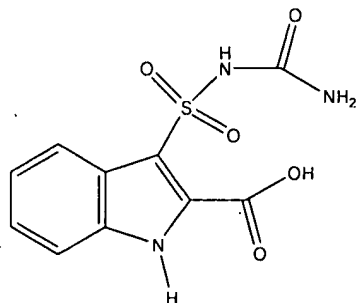
n is 0 to 6;

w is 0 to 4; and

R^5 is defined in claim 1.

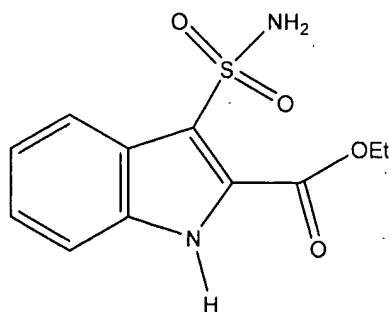
Determination of the scope and content of the prior art (MPEP §2141.01)

Szmuszkovicz (U.S. Patent 3,180,875) discloses a compound of formula



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Szmuszkovicz, *Journal of Organic Chemistry* (1964), 29(1), p178-84 discloses a



compound of formula

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Szmuszkovicz (U.S. Patent 3,180,875) teaches a specific compound with carboxylic acid attaching on indole 2-position. However, Szmuszkovicz does not teach a compound with carboxylic acid ester (such as methyl or ethyl ester) in the patent.

Szmuszkovicz (*Journal of Organic Chemistry*, 1964, 29(1), p178-84) teaches a specific compound with carboxylic acid ethyl ester attaching on indole 2-position. However, Szmuszkovicz does not teach a compound with carboxylic acid (such as methyl or ethyl ester) in the article.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Some of the instantly claimed compounds would have been obvious over Szmuszkovicz compound having carboxylic acid vs. carboxylic acid ester. To those skilled in the chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. *In re Henze*, 85 USPQ 261 (1950). Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claim Objections

Claims 1-6 are objected to for containing elected and non-elected subject matter. The elected subject matter has been identified supra.

Conclusions

No claim is allowed.

Telephone Inquiry

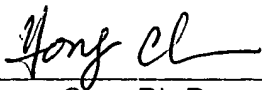
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu whose telephone number is 571-272-5759. The examiner can normally be reached between 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

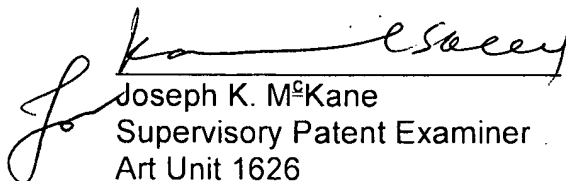
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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